REMARKS

The undersigned would like to thank the Examiner and the Supervisor Primary Examiner for the helpful discussion that the undersigned had with them on August 16, 2006. The undersigned notes that the Examiner did not issue an Advisory Action, summarizing the meeting. The undersigned would summarize the meeting as follows: On August 16, 2006, Examiner Ford, Supervisor Examiner Lynette Smith and David Marks talked over the telephone about the claims and prior art. No agreement was reached as to the allowability of claims.

The undersigned hopes that this summary accurately reflects the meeting.

The Applicants are requesting the entry of the following amendments to Claim 21.

The Applicants request the removal of the language "wherein said *Fusobacterium necrophorum* whole cell culture remains non-concentrated" and the word "unconcentrated" from Claim 21.

The Applicants request the addition of the phrase "and wherein said *Fusobacterium necrophorum* whole cell culture contains the growth medium in which said *F. necrophorum* is grown" to Claim 21. This phrase is being added to indicate more clearly that the step of inactivating the *F. necrophorum* includes not just the bacteria but also the growth medium in which the bacteria are grown. Support for this amendment can be found in the Specification on pages 7-9 and in Example 1 on pages 11-12. In pages 7-9, the Specification discuss that the bacteria are grown in various types of medium, that the bacteria should be grown *in-vitro* in the medium to allow for the production of antigens, that the most preferred method for forming sufficient bacterial culture is to grow the bacteria in culture medium in flasks (indicating that the culture medium is liquid and not a solid), that production cultures are grown in culture vessels (flasks) for about 10 to about 18 hours, that formaldehyde is added to the inactivate the bacteria, that the "inactivated whole cell culture" may be used for production or stored until needed for production, and that one can "harvest [the bacteria] using any technique known to be sufficient to recover at least 1 x 10^8 CFUs/ml, e.g., pipetting the culture out of the flask or device in which the culture was grown." In Example 1 on pages 11-12, the Specification makes clear that the bacteria production cultures are grown and inactivated by the addition of formaldehyde, and that "[t]o form the vaccine the killed whole bacteria culture was gently stirred and the adjuvant... was slowly added to the suspension..." These passages indicate that the bacteria growth medium is incorporated into the vaccine, along with the bacteria cells; and that both are inactivated with formaldehyde.

<u>35 U.S.C. § 112 first paragraph</u>

The Examiner rejected Claims 21-22 under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the Specification as to reasonably convey to one skilled in the art that the inventors were in possession of the claimed invention at the time of filing of the application. The Examiner felt that the terms "non-concentrated" and "unconcentrated" in Claim 21 is new matter. The Examiner requested that the Applicant either point out where in the Specification there is support for this amendment or cancel it.

The Applicants have amended Claim 21 to remove the language that the Examiner believed was problematic. Thus, this rejection is moot and the Applicants request that the Examiner withdraw this rejection.

35 U.S.C. § 112 second paragraph

The Examiner rejected Claims 21-22 under 35 U.S.C. § 112, second paragraph because the Examiner felt that the terms "non-concentrated" and "unconcentrated" is unclear.

The Applicants have amended Claim 21 to remove the language that the Examiner believed was problematic. Thus, this rejection is moot and the Applicants request that the Examiner withdraw this rejection.

35 U.S.C. § 103(a)

The Examiner maintained the rejection of Claims 21-22 under 35 U.S.C. § 103(a) as being obvious because of Garcia et al. in light of Emery et al. The Examiner felt that Garcia et al. teaches a whole cell bacterin of *Fusobacterium necrophorum* cells to prevent liver abscesses, but does not teach using a whole cell bacterin of *F. necrophorum* to prevent footrot. The Examiner felt that Emery et al. supplies that missing item because the Examiner felt that Emery et al. teaches that *F. necrophorum* causes footrot and that *F. necrophorum* can be cultured in a suitable medium for up to 18 hours. The Examiner felt that it would be prima facie obvious that the vaccine composition comprising *F. necrophorum* would be effective in preventing infections caused by *F. necrophorum* because Garcia et al. has shown that *F. necrophorum* is effective against preventing liver abscesses caused by *F. necrophorum* infections.

The Applicants respectfully disagree with the Examiner about the teachings of Garcia et al. because Garcia et al. does not teach a whole cell bacterin of *F. necrophorum*. Rather, Garcia et al. teaches using sonicated cells of *F. necrophorum* in a vaccine. In the first full sentence of 2nd column, page 223 of Garcia et al. states "Cells were ruptured ultrasonically for

18-20 min in a MSE 100 sonic vibrator." The second sentence states "An almost complete disruption of the cells by this technique was observed by phase microscopy." This shows that "sonication" means "ruptured cells" – the bacteria cells are not "whole".

At the bottom of page 223, 2nd column, and the top of 224, 1st column, Garcia et al. explains the four groups of calves treated. Group 1 was the negative control; the calves did not receive any vaccine. Group 2 calves received just the adjuvant, no bacteria. Group 3 calves were vaccinated with a "sonicated cell toxoid" (p. 224) which was ruptured cells; not "whole" cells. Group 4 calves received "cytoplasmic toxiod" (p. 224) which was ruptured cells that were then "centrifuged at 18,000 x g for 15 min and separated into the supernatant and sediment. The supernatant was considered to consist of the intracellular or cytoplasmic fraction and was designated as such." (2nd column, first paragraph, p. 223) Thus, a careful reading of Garcia et al. reveals that Garcia et al. never administered whole bacteria to calves to prevent or treat liver abscesses.

Emery et al. does not teach a method of preventing liver abscesses and footrot by administering using whole cells of *Fusobacterium necrophorum* to bovine.

There is no suggestion in either Garcia et al. or Emery et al. that one can prevent liver abscesses and footrot in cattle by administering whole cells of *F. necrophorum* to the cattle. These articles do not suggest or teach this concept individually nor in combination. As such, the Applicants respectfully believe that this 103(a) rejection is incorrect and request that the Examiner withdraw it.

The Examiner also maintained the rejection of Claims 21-22 under 35 U.S.C. § 103(a) as obvious over Garcia et al. in light of Clark et al. The Examiner stated that Garcia et al. teaches a method of preventing liver abscesses in bovines using a vaccine preparation of *S. necrophorus* inactivated with formaldehyde. The Examiner noted that Garcia et al. teaches a vaccine adjuvated with alum, and the dose volume from 1.0 to 20 ml. The Examiner stated that Garcia et al. teaches providing a prime + booster administration and the booster's volume is 5.0 ml. The Examiner noted that Garcia et al. does not teach a method of preventing footrot. The Examiner believed that Clark et al. teaches that *F. necrophorum* is effective in preventing footrot. According to the Examiner, Clark et al. teaches a vaccine of whole cultures, cytoplasmic fractions, cell-free supernatants or killed cells formulated in mineral oil adjuvant. The Examiner felt that it would be prima facie obvious to add the vaccine compositions comprising the culture supernatants of *F. necrophorum* taught by Clark et al. to the vaccine compositions comprising *F. necrophorum* cytoplasmic toxiod of Garcia et al. to be used to prevent footrot and liver abscesses in cattle.

In response to Applicants prior arguments, the Examiner stated that Clark et al. teaches vaccine compositions comprising *F. necrophorum* whole cell cultures and that *F. necrophorum* causes footrot. The Examiner believes that there is nothing on record to suggest that the

combination of references do not teach the claimed invention. The Examiner believed that Garcia et al. teaches a vaccine prepared from "sonicated unfractionated cells (whole cells)" and that both articles teach vaccine compositions comprising whole cell cultures. Thus, the articles do not teach away from the Applicants' invention.

The Applicants respectfully disagree with the Examiner's characterization of Clark et al. and Garcia et al. and the combination of the two articles.

As noted above, the Applicants believe that Garcia et al. fails to teach "whole cells" in the vaccine. Garcia et al. teaches using sonicated cells which are "ruptured" in vaccines. Garcia et al. uses two types of vaccines, one which is sonicated cells that include all components of the sonicated cells, and the other which is the cytosolic fraction of the sonicated cells. See Garcia et al. at the bottom of page 223, 2nd column, and the top of 224, 1st column.

Thus, the Examiner's argument that Garcia et al. teaches using "whole cells" in a vaccine to prevent liver abscesses is incorrect. This error alone is enough to make the Examiner's rejection moot because if Garcia et al. fails to teach a vaccine containing whole *F. necrophorum* for the treatment of liver abscesses, then the combination of Garcia et al. and Clark et al. cannot make the Applicants' invention prima facie obvious. There is no teaching in Clark et al. that provides what Garcia et al. lacks.

However, the Applicants believe that Clark et al. was also mischaracterized by the Examiner. On page 107, second column, for Experiment 1, Clark et al. made three types of vaccines: Vaccine # 1 contained *F. necrophorum* cells that were "concentrated 10 times" because the bacteria cells were passed through a XM100 A membrane with a molecular weight retention factor of 100,000, leading to a 10x concentration of the bacteria. Vaccine #2 was made from *F. necrophorum* cytoplasmic fraction, that is the bacteria were sonicated and centrifuged, just like in Garcia et al. and the supernatant fraction after centrifugation was used to make the vaccine. Vaccine # 3 contained "cell-free culture supernatant fluid that had been concentrated 10 times using a XM100 A membrane". In Experiment 3, on page 108, Clark et al. made two vaccines. The first vaccine contained "cell-free culture supernatant fluid that had been concentrated 10 times" using the XM100 A membrane. The second vaccine contained bacteria cells that had been washed three times by centrifugation and then suspended in phosphate buffered saline. Thus, Clark et al. does not make a vaccine using bacteria and bacteria media that was "unconcentrated". By concentrating the bacteria during the filtration step, Clark et al. removes some material from the culture medium prior to making a vaccine.

In contrast, the Applicants' invention does not contain a concentration step and uses the entire culture medium in which the bacteria grow in the vaccine. The Applicants' Specification does not teach a concentration step. The Applicants have made this distinction more evident with the amendment to Claim 21, by stating that the whole cell culture contains the growth medium in which said *F. necrophorum* is grown. This amendment indicates that one uses the

bacteria and an unconcentrated growth medium with nothing during the inactivation step and in the vaccine.

Because Clark et al. teaches a vaccine containing concentrated bacteria cells and because Garcia et al. fails to teach a vaccine containing whole bacterial cells for the treatment of liver abscesses, the Applicants believe that Garcia et al. and Clark et al. in combination fail to teach the Applicants' invention. Clark et al. fails to supply the missing elements, that one can use whole cells and unconcentrated medium for the prevention of liver abscesses and footrot.

As such, the Applicants request that the Examiner withdraw this rejection.

Applicants believe that all pending claims are allowable and requests allowance.

Any questions or issues can be directed to the below signed attorney at this address. Thank you for your assistance with this matter.

Respectfully submitted,

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